K111914

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510(k) SUMMARY

Virtual Slide System
OLYMPUS VS800 System, VS800HER2 MR Application

1 General Information

- Applicant:

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Establishment Registration No.: 8010047

- Contact Person:

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- Manufacturer:

OLYMPUS CORPORATION
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Nagano-prefecture 396-0026, Japan
Establishment Registration No.: 9614612

2 Device Identification

- Device Trade Name: Virtual Slide System, OLYMPUS VS800 System, VS800 HER2 MR Application
- Regulation Number: 21CFR 864.1860
- Regulation Name: Immunohistochemistry reagents and kits.
- Regulatory Class: II
- Classification Panel: Pathology
- Product Code: OEO

3 Predicate Device Information

Device Name	510(k) No.	Manufacturer
ScanScope XT System	K071671	Aperio Technologies, Inc.

4 Device Description

The VS800 System is an automated digital slide creation, management and viewing system. The VS800 System components consist of an automated digital microscope slide scanner (VS800-SS) which include a computer, keyboard and mouse, operating monitor (VS800-MTR) and VS Viewer software (VS2-ASW-IDB). The system capabilities include digitizing microscope slides at high resolution, storing and managing the resulting digital slide images, retrieving and displaying digital slides, including support for remote access over wide-area networks, providing facilities for annotating digital slides and entering and editing metadata associated with digital slides, and facilities for image analysis of digital slides. The remote digital slide viewing capabilities of the system support reading digital slides on a computer monitor, enabling Pathologists to make clinically relevant decisions analogous to those they make using a conventional microscope. Specifically, the system supports the pathologist in the detection of HER2/neu by manual examination of the digital slide of formalin-fixed, paraffin-embedded normal and neoplastic tissue immunohistochemically stained for HER2 receptors on a computer monitor.

The VS800-SS (an automated digital microscope slide scanner) creates high resolution, color digital slide images of entire glass slides in a matter of minutes. High numeric aperture 20x objectives, specially designed for VS800-SS optical system and real time contrast auto focus system (AF) are used to produce high-quality images. VS800-SS employs a 2D CCD imager for fine image acquisition which is same technologies used in conventional microscope imaging system. VS800-SS captured image is as same as conventional microscope image.
The VS-ASW-IDB (VS Viewer software) is a full-featured digital pathology information management system. The software runs on a server computer, which stores digital slide images on disk storage such as a RAID array, and which hosts an SQL database that contains digital slide metadata. The VS-ASW-IDB includes a web application and services which encapsulate database and digital slide image access for other computers. The VS-ASW-IDB also includes support for locally or remotely connected Image Server, which run digital slide viewing software provided as part of VS-ASW-IDB.

The laboratory technician or operator of VS800-SS loads glass microscope slides into a specially designed slide carrier with a capacity up to 100 slides per carrier (300 total). The scanning process begins when the operator starts the VS800-SS scanner and finishes when the scanner has completed scanning of all loaded slides. As each glass slide is processed, the system automatically stores stitched images as a single digital slide image, which represents a histological reconstruction of the entire tissue section. When the slide scanning finished, then operator of scanner will confirms the image quality and records to the database. When the images are recorded, pathologists or authorized parsons can observe these images to access the VS-ASW-IDB.

5 Indications for Use

The VS800 system is an automated digital slide creation, management, and viewing system. It is intended for in vitro diagnostic use as an aid to the pathologist in the display, detection, counting and classification of tissues and cells of clinical interest based on particular color, intensity, size,

pattern and shape.

The VS800HER2 Manual Read (MR) of digital slide application is intended for use as an aid to the pathologist in the detection and semi-quantitative measurement of HER2 by manual examination of the digital slide of formalin-fixed, paraffin-embedded and neoplastic tissue IHC stained for HER2 receptors on a computer monitor. HER2 results are indicated for use as an aid in the management, prognosis and prediction of therapy outcomes of breast cancer.

The VS800HER2 MR of digital slide application is intended for use as an accessory to the DakoHercepTest to aid the pathologist in the detection and semi-quantitative measurement of HER2 by manual examination of the digital slide of formalin-fixed, paraffin-embedded and neoplastic tissue immunohistochemically stained for HER2 receptors on a computer monitor. When used with the Dako Hercep Test, it is indicated for use as an aid in the assessment of breast cancer patients for whom HERCEPTIN® (Trastuzumab) treatment is being considered.

Note: The actual correlation of the Dako Hercep Test to the Herceptin® clinical outcome has not been established.

6 Comparison of Technological Characteristics

A summary of the technological characteristics of the VS800 System, subject device, in comparison to the predicate device follows:

Method of cell detection: The method of cell detection is by colorimetric pattern recognition by microscopic examination of prepared cells by size, shape, hue and intensity as observed by a computer-automated, microscopic digital slide scanner system and/or by visual observation by a health care professional.

System Components: The system components comprising the VS800 System, subject device, are substantially equivalent to those in the predicate device; i.e., a computer-automated digital microscope slide scanner, computer, color monitor, and keyboard.

Energy Source: The electrical service is 100 - 120vAC / 220 - 240vAC, 50Hz/60 Hz, 5.8A MAX, which is similar to the predicate device electrical service requirements.

7 Summary of Non-Clinical Testing

In support of the non-clinical tests, a risk analysis was carried out in accordance with established in-house acceptance criteria based on ISO 14971. The design verification tests and their acceptance criteria were identified and performed as a result of the risk analysis assessment. In addition, electrical safety and electromagnetic compatibility testing was performed and carried out in accordance to IEC61010-2-101:2002 and EN 61326-2-6:2006.

The software validation activities were performed in accordance with the FDA Guidance, "Guidance for the Contents of Premarket Submissions for Software Contained in Medical Devices." Olympus has accessed that our proposed VS800 System has a Moderate Level of concern, and the

documents within the 510(k) support the level of concern.

8 Summary of Clinical Testing

A prospective clinical study was conducted to validate the performance for reading images of slides on a computer monitor (manual digital reads) in comparison to reading the glass-slides with a conventional microscope (manual microscopy reads). The VS800 system was used to digitize, manage and view the slides. The specific application is limited to Formalin-Fixed, Paraffin-Embedded (FFPE) breast tissue specimens ImmunoHistoChemically (IHC) stained with Human Epidermal growth factor Receptor 2 (HER2) using DakoCytomation's FDA approved HercepTest™ kit.

A study was conducted at two clinical sites to compare the performance of manual digital reads with manual microscopy reads. One clinical laboratory provided two clinical sites with different slide sets of one hundred (100) slides each. The slides were selected from archive to provide an equal distribution of HER2 scores in the trichotomous categorization of the HER2 scores combining 0 and 1+, and leaving 2+ and 3+ uncombined, and then re-cut and re-stained. At each clinical site, three different pathologists performed first a blinded read of the glass-slides using a conventional microscope. Then, the slides were digitized using a different instrument at each clinical site, and after a wash-out period of at least one week and randomization, the same three pathologists at each site performed another blinded read of the slides, but this time they read the images of the slides on their computer monitors.

The statistical analysis is presented across all slides comparatively between manual microscopy reads and manual digital reads using Percent Agreement (PA) with a 95% Confidence Interval (CI). The statistical analysis is provided for a trichotomous agreement of the HER2 scores combining 0 and 1+, and leaving 2+ and 3+ uncombined, as suggested by FDA.

Tables 1, 2, 3, 4, 5, and 6 show the 4x4 tables for the agreements between the manual microscopy reads and manual digital reads using column-wise Percent Agreement (PA; i.e., percent of manual digital reads that agree with a given manual microscopy read) with a Exact 95% Confidence Interval (CI) for each of the three pathologists at site 1 and site 2. For example, there were 33 (10 + 23) slides with manual microscopy read either 0 or 1+ and 30 (4 + 0 + 6 +20) of these were called 0 or 1+ by manual digital read, resulting in a PA of 90.91% (30/33).

Pathologist 1		Manual Microscope Read				
		0	1+	2+	3+	TOTAL
Manual Digital Read	0	4	0	0	0	4
	1+	6	20	3	0	29
	2+	0	3	30	1	34
	3+	0	0	1	32	33
	TOTAL	10	23	34	33	100

Score	PA	Exact 95% CI
0, 1+	90.91%	(75.67%, 98.08%)
2+	88.24%	(72.55%, 96.70%)
3+	96.97%	(84.24%, 99.92%)

Table 1:
Manual Microscopy Reads vs. Manual Digital Reads – Site 1
4x4 Tables for Pathologist 1

Pathologist 2		Manual Microscope Read				
		0	1+	2+	3+	TOTAL
Manual Digital Read	0	8	1	0	0	9
	1+	5	17	3	0	25
	2+	0	3	30	1	34
	3+	0	0	0	32	32
	TOTAL	13	21	33	33	100

Score	PA	Exact 95% CI
0, 1+	91.18%	(76.32%, 98.14%)
2+	90.91%	(75.67%, 98.08%)
3+	96.97%	(84.24%, 99.92%)

Table 2:
Manual Microscopy Reads vs. Manual Digital Reads – Site 1
4x4 Tables for Pathologist 2

Pathologist 3		Manual Microscope Read				
		0	1+	2+	3+	TOTAL
Manual Digital Read	0	3	0	0	0	3
	1+	0	12	1	0	13
	2+	0	10	35	5	50
	3+	0	0	0	34	34
	TOTAL	3	22	36	39	100

Score	PA	Exact 95% CI
0, 1+	60.00%	(38.67%, 78.87%)
2+	97.22%	(85.47%, 99.93%)
3+	87.18%	(72.57%, 95.70%)

Table 3:
Manual Microscopy Reads vs. Manual Digital Reads – Site 1
4x4 Tables for Pathologist 3

Pathologist 1		Manual Microscope Read				
		0	1+	2+	3+	TOTAL
Manual Digital Read	0	9	2	0	0	11
	1+	2	10	1	0	13
	2+	1	3	34	0	38
	3+	0	0	7	31	38
	TOTAL	12	15	42	31	100

Score	PA	Exact 95% CI
0, 1+	85.19%	(66.27%, 95.81%)
2+	80.95%	(65.88%, 91.40%)
3+	100%	(88.78%, 100%)

Table 4:
Manual Microscopy Reads vs. Manual Digital Reads – Site 2
4x4 Tables for Pathologist 1

Pathologist 2		Manual Microscope Read				
		0	1+	2+	3+	TOTAL
Manual Digital Read	0	15	0	1	0	16
	1+	2	12	4	0	18
	2+	0	1	29	0	30
	3+	0	0	3	33	36
	TOTAL	17	13	37	33	100

Score	PA	Exact 95% CI
0, 1+	96.67%	(82.78%, 99.92%)
2+	78.38%	(61.79%, 90.17%)
3+	100%	(89.42%, 100%)

Table 5:
Manual Microscopy Reads vs. Manual Digital Reads – Site 2
4x4 Tables for Pathologist 2

Pathologist 3		Manual Microscope Read				
		0	1+	2+	3+	TOTAL
Manual Digital Read	0	11	1	0	0	12
	1+	3	8	0	0	11
	2+	0	13	25	2	40
	3+	0	0	6	31	37
	TOTAL	14	22	31	33	100

Score	PA	Exact 95% CI
0, 1+	63.89%	(46.22%, 79.18%)
2+	80.65%	(62.53%, 92.55%)
3+	93.94%	(79.77%, 99.26%)

Table 6:
Manual Microscopy Reads vs. Manual Digital Reads – Site 2
4x4 Tables for Pathologist 3

In addition, a precision study was conducted at one clinical site to assess the intra-instrument and inter-instruments precision for manual digital reads. A subset of thirty (30) slides from the comparison with conventional microscopy study was used. The slides were selected to provide an equal distribution of HER2 scores in the trichotomous categorization of the HER2 scores combining 0 and 1+, and leaving 2+ and 3+ uncombined. For comparison, a pathologist reads first the thirty (30) glass-slides three times using the same conventional microscope. Then, the same pathologist reads the images of the thirty (30) glass-slides three times on a computer monitor, re-scanned each times on the same instrument. Finally, the same pathologist reads the images of the thirty (30) glass-slides another three times on a computer monitor, this time the slides were re-scanned each time on a different instrument. The wash-out period between reads were at least one week and the slides were randomized between reads.

The statistical analysis is presented for intra- and inter-instruments variations, using Percent Agreement (PA) with a 95% Confidence Interval (CI). The statistical analysis is provided for a trichotomous categorization of the HER2 scores combining 0 and 1+, and leaving 2+ and 3+ uncombined. Table 7 shows the overall agreements across all slides and all pair wise comparisons of the different reads.

	PA	95% CI
Intra-Instrument	100%	(95.98, 100)
Inter-Instruments	95.6%	(89.01, 98.78)

Table 7: Overall Agreements for
the Precision of Manual Digital Reads.

The intra-instrument intra-pathologist agreement for manual digital reads is 100% with a 95% confidence interval from 95.98% to 100%. The inter-instruments intra-pathologist agreement for manual digital reads is 95.6% with a 95% confidence interval from 89.01% to 98.78%.

9 Conclusion

In summary, as results of the above evaluations for comparing to the predicate device, the subject device, OLYMPUS VS800 System do not incorporate any significant changes that could affect the safety or effectiveness of the device.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

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AUG 21 2012

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c/o Ms. Sheri L. Musgnung
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Re: k111914
Trade/Device Name: Olympus Virtual Slide System, VS800 System, VS800 HER2 Manual Read (MR) application
Regulation Number: 21 CFR 864.1860
Regulation Name: Immunohistochemistry reagents and kits
Regulatory Class: Class II
Product Code: OEO
Dated: August 13, 2012
Received: August 15, 2012

Dear Ms. Musgnung:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Maria M. Chan

Maria M. Chan, Ph.D.
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number: K111914

Device Name: Virtual Slide System, Olympus VS800 System, VS800 HER2 MR Application

Indications for use:

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Note: The actual correlation of the Dako Hercep Test to the Herceptin® clinical outcome has not been established.

Prescription Use ✓ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k) K111914